CASE REPORT

A 30-year-old, 14 weeks pregnant South Indian woman presented to our emergency department with confusion, diplopia, blurring of vision, gait ataxia, nystagmus and conjugate gaze palsy with a background of intractable hyperemesis gravidarum. With clinical suspicion and radiological confirmation, she was diagnosed to have Wernicke’s encephalopathy. Immediate intervention with parenteral thiamine restored her neurological status with amelioration of nystagmus, diplopia and ataxia without any neurological sequelae. Here we report this case to illustrate the importance of early recognition of this extremely rare illness in order to avoid permanent neurological deficit.

DISCUSSION

Wernicke’s encephalopathy (WE) is a neurological disorder caused by thiamine deficiency. It is an acute, neuropsychiatric syndrome, characterised by nystagmus and ophthalmoplegia, mental status changes and unsteadiness of stance and gait – although this triad is seen in only 16% of patients. 1

Carl Wernicke described this distinctive entity in 1881 as an acute superior haemorrhagic polioencephalitis in two alcohol-misusing men and a young woman who developed persistent vomiting due to pyloric stenosis after the ingestion of sulphuric acid. 2 Wernicke’s encephalopathy is more common in males than in females (male/female ratio 1.7:1). 1 The estimated mortality is 17%. 1 Most patients with WE have a background of alcohol abuse. Non-alcoholic WE is an uncommon disorder of the central nervous system. Recurrent vomiting and chronic diarrhoea may result in WE. Persistent and severe nausea and vomiting in pregnancy that can progress to hyperemesis gravidarum is an extremely rare cause of WE. Wernicke’s encephalopathy was recognised as a complication of hyperemesis of pregnancy in 1914. 4

ABSTRACT

Wernicke’s encephalopathy is a potentially fatal but readily reversible medical emergency caused by thiamine deficiency. A 30-year-old, 14 weeks pregnant South Indian woman presented with confusion, diplopia, blurring of vision, gait ataxia, nystagmus and conjugate gaze palsy with a background of intractable hyperemesis gravidarum. With clinical suspicion and radiological confirmation, she was diagnosed to have Wernicke’s encephalopathy. Immediate intervention with parenteral thiamine restored her neurological status with amelioration of nystagmus, diplopia and ataxia without any neurological sequelae. Here we report this case to illustrate the importance of early recognition of this extremely rare illness in order to avoid permanent neurological deficit.

KEYWORDS

Hyperemesis gravidarum, Wernicke’s encephalopathy

DECLARATION OF INTERESTS

No conflict of interests declared.
Thiamine, a water-soluble essential vitamin obtained from diet, is an important cofactor for three key enzymes involved in both the Krebs and pentose phosphate cycle – ketoglutarate dehydrogenase complex, pyruvate dehydrogenase complex and transketolase. It is also essential in maintaining osmotic gradients across cell membranes.

Thiamine deficiency leads to impaired cerebral energy metabolism, focal lactic acidosis, N-methyl-D-aspartate receptor-mediated excitotoxicity, blood–brain barrier breakdown and decreased osmotic gradients across cell membranes. This pathophysiologic abnormality is prone to occur in the periventricle and periaqueductal regions in which thiamine-related glucose and oxidation metabolism is abundant. Ophthalmoplegia and ataxia ensue from the involvement of the pontine and mesencephalic tegmentum. Hypomnesia and global confusion are related to damage within the thalami and possibly to damage to the mammillary bodies. Thiamine deficiency may occur in pregnancy, even with standard prenatal thiamine supplementation, and, if inadequately treated, hyperemesis gravidarum may lead to WE, central pontine myelinolysis and death.

There is no specific routine laboratory test available, and no specific diagnostic abnormalities have been revealed in cerebrospinal fluid, brain imaging, electroencephalogram or evoked potentials. Wernicke’s encephalopathy remains a clinical diagnosis. The presumptive diagnosis of WE can be confirmed by determining blood thiamine concentrations or by measuring the red blood cell transketolase activity. Recently, an isocratic high-performance liquid chromatography method for the assessment of thiamine, thiamine monophosphate and thiamine diphosphate in human erythrocytes has been described.

In our case, the circulating levels of thiamine and transketolase activity were not measured due to an unavailability of the tests. These tests are not generally available routinely on an emergency basis. However, even if they were, it is more important to make a presumptive diagnosis of WE and treat the patient as soon as possible.

Magnetic resonance imaging is currently considered the most valuable method to confirm a diagnosis of WE. It has a sensitivity of only 53% but a high specificity of 93%. Magnetic resonance imaging studies typically show an increased T2 signal, bilaterally symmetrical, in the paraventricular regions of the thalamus, the hypothalamus, mammillary bodies, the periaqueductal region, the floor of the fourth ventricle and midline cerebellum. The diagnosis is clinical and mainly supported by the dramatic response of neurological signs to parenteral thiamine.

The MRI signal characteristics and lesion sites are not entirely specific for WE. The possible causes of acute encephalopathies need to be differentiated, particularly...
when the clinical history does not reveal a definite predisposing factor related to WE or when the response of neurological signs to the administration of thiamine is unclear.

The differential diagnosis includes paramedian thalamic infarction (top-of-the-basilar syndrome), ventriculo-encephalitis, Miller-Fisher syndrome, primary cerebral lymphoma, Behçet’s disease, multiple sclerosis, Leigh’s disease, variant Creutzfeldt-Jakob disease, paraneoplastic encephalitis, severe hypophosphataemia, acute intoxication from methyl bromide and chronic intoxication from bromovalerylurea.8–11

The typical MRI findings are similar in alcoholic and non-alcoholic patients with WE, but the atrophy of the cerebellar vermis and mammillary bodies differs between these two. This is due to the following reasons:

1. Cerebellar vermis and mammillary bodies are susceptible to thiamine deficiency in alcoholic patients;
2. MRI findings in the acute phase are contaminated by previous attacks in alcoholics.

Magnetic resonance imaging is helpful not only to diagnose acute non-alcoholic WE but also to evaluate the pathologic evolution and prognosis of the disorder. The disorder has a good prognosis if only the periaqueductal area, thalamus and caudate nucleus are involved. Cortical damage may be indicative of irreversible damage and poor prognosis.12

In a study by Chiossi and colleagues,13 the overall pregnancy loss rate directly (spontaneous fetal loss) and indirectly (planned abortion) attributable to WE was 46.9% (23/49). The classical Wernicke’s triad (confusion, ocular abnormalities and ataxia) manifested in only 46.9% (23/49) of the patients. Confusion affected 63.3% (31/49) of the patients, ocular signs 95.9% (47/49) and ataxia 81.6% (40/49). Deterioration of consciousness affected 53.1% (26/49) of the subjects and memory impairment 61.2% (30/49). A complete remission of the disease occurred in only 14 of 49 cases.13

Any pregnant women who develop hyperemesis should receive thiamine supplementation, especially before intractable nausea and vomiting for four weeks in her local village hospital with IV fluids with dextrose, without complications of vitamin B deficiency in patients undergoing alcohol withdrawal in the community, high dose oral thiamine (200 mg per day), together with vitamin B strong tablets (30 mg per day), is the treatment of choice.14

The only available intravenous (IV) treatment that includes thiamine (B1), riboflavin (B2), pyridoxine (B6) and nicotinamide is Pabrinex. It is given as two pairs of vials of Pabrinex 1 and 2 diluted in 100 ml of crystalloid and should be given IV over 30 minutes. If the patient is admitted, consider two pairs of vials three times daily for two days IV, to be followed, if there is any improvement, by one pair per day for five days (IV or intramuscular) at the discretion of the admitting team.

The ocular signs in our patient may have been due to the involvement of midbrain gaze centres. The lesions in the cerebellar vermis may have accounted for the ataxia.

The treating physicians should have a high index of suspicion of WE in patients with hyperemesis, starvation, dialysis, cancer, magnesium depletion, AIDS, gastroplasty/gastric bypass surgery, rapid weight loss, anorexia nervosa, refeeding syndrome or prolonged intravenous feeding. Failure to diagnose WE and to institute adequate parenteral therapy results in death in 20% of patients; 75% will be left with permanent brain damage involving severe short-term memory loss (Korsakoff’s psychosis).15

CONCLUSION

Hyperemesis gravidarum is an extremely rare cause of WE. A diagnosis of WE should be suspected once any one of the neurological triad is presented in a patient with hyperemesis gravidarum.

This case, in which the patient had been treated for intractable nausea and vomiting for four weeks in her local village hospital with IV fluids with dextrose, without thiamine supplementation, illustrates the importance of early recognition and treatment of this rare illness. We therefore emphasise the importance of thiamine supplementation in hyperemesis in pregnancy in order to avoid permanent neurological deficit and possible maternal and fetal mortality.

REFERENCES

5 Martin PR, Singleton CK, Hiller-Sturmofof S. The role of thiamine...

RCPE/RCPCH JOINT SYMPOSIUM

ADOLESCENT HEALTH: EVERYONE'S PROBLEM

Thursday 24 September 2009 at the RCPE

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- Adolescent health issues in medicine: current issues
  *Dr Janet McDonagh*
- Psychological issues for adolescents
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- Adolescent health in Scotland: national strategy
  *Mr Morgan Jamieson*

**Session 2 Health risks: role of the professional**
- Cardiovascular disease risk: who should we treat and how?
  *Dr Ian Wilkinson*
- Reproductive health risks

**Session 3 Legal issues**
- Medico-legal issues
  *Mr Michael Handley*
- Sexually active 13-year-old girl taken overdose: what do you do?

**Session 4 Transition**
- Experience of a transition service: how to do it in cystic fibrosis service?
  *Dr Tom Marshall*

**Case studies**
- Teenager with type 1 diabetes mellitus presenting with severe diabetic ketoacidosis (DKA): how do we improve outcome? How do we reduce the rate of DKA?
  *Dr Brian Kennon*
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